REMARKS

Claims 1, 2 and 4-20 are pending in the instant application. Claims 1, 2 and 4-20 have been rejected. Claims 11 and 16-20 have been canceled. Claims 1 and 15 have been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims Under 35 U.S.C. 112, First Paragraph

Claim 11 has been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner suggests that this claim is drawn to a compound which hybridizes with an active site which is not defined in a way in the specification that allows one to understand how it is experimentally determined. Applicants have canceled claim 11. Therefore, withdrawal of this rejection is respectfully requested.

Claims 15-20 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art

to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The Examiner acknowledges that the specification while being enabling for antisense inhibition of CD36L1 expression *in vitro* does not reasonably provide enablement for *in vivo* antisense inhibition of expression of CD36L1; the Examiner cites several articles to support this position. Applicants respectfully traverse this rejection of the claims.

Applicants disagree with the Examiner's suggestion that cited references support the position that application of antisense *in vivo* is highly unpredictable.

The Examiner has pointed to articles concerning the technology of antisense oligonucleotides to support the view that antisense technology is unpredictable. However, when one reads each of the papers as a whole, as required under MPEP 2141.02, these references actually teach the potential usefulness of this class of drugs in humans, and more importantly fail to provide any reasonable basis to doubt the pharmacological activity observed in cells in the instant invention would also occur in cells in animals and humans. f studies presented in the instant specification. Therefore, what these papers cited by the Examiner actually teach is that antisense oligonucleotides must be developed using well designed studies that

progress logically from activity in cells to activity in animals and humans. Nowhere in the references cited do the authors state or suggest that results of well-designed *in vitro* pharmacological studies would not be predictive of activity *in vivo*.

The paper by Braasch and Corey (2002) describes the advances that have been made in the design of antisense compounds over the years. Included in the discussion are the types of advances that are taught in the specification as filed. Nowhere in the reference do the authors state or suggest that results of well-designed *in vitro* pharmacological studies would not be predictive of activity *in vivo*. In fact, the paper states in the abstract that success in clinical trials with these agents has occurred.

The paper by Tamm et al. (2001) is another more recent review of the antisense technology and its specific application to oncology. Again, although the use of antisense is discussed in terms of what can go wrong, the paper again describes advances such as those taught in the instant specification. Nowhere in the reference do the authors state or suggest that results of well-designed *in vitro* pharmacological studies would not be predictive of activity *in vivo*.

The paper by Branch (1998) teaches the need to develop antisense molecules based on sound data and careful screening, such as is presented in the instant specification. Nowhere does the paper state that extrapolation from *in vitro* data to *in vivo* effects is unpredictable.

The papers by Gewirtz et al. (1996) and Agrawal (1996) are older papers not relevant to the state of the art of antisense compounds in 2001, the filing date of the instant application. Both papers discuss in general terms issues that were related to older antisense technology. However, nowhere do these papers state that extrapolation from *in vitro* data to *in vivo* effects is unpredictable.

However, Applicants have amended claim 15 to recite that the method is performed *in vitro* in an earnest effort to advance the prosecution and facilitate the allowance of this case. Claims 16-20 have been canceled with Applicants reserving the right to file a continuing application directed to this subject matter without prejudice. Withdrawal of the rejection is requested in light of these amendments.

II. Rejection of Claims Under 35 U.S.C. 102(b)

Claims 1 and 2 have been rejected under 35 U.S.C. 102(b) as being anticipated by Acton et al. (US Patent No. 5,965,790). The Examiner suggests that this patent teaches antisense compounds that target and inhibit expression of CD36L1. Applicants respectfully traverse this rejection.

At the outset, Applicants have amended claim 1, and by dependency claim 2, to refer to antisense compounds targeted to specific regions of a CD36L1 nucleic acid molecule specified by SEQ ID NO. Support for these amendments can be found throughout the specification as filed but in particular at pages 87-90.

Acton et al. (US Patent 5,965,790) discloses an isolated nucleic acid molecule which is capable of hybridizing to a nucleic acid molecule consisting of the nucleotide sequence of the human CD36L1 promoter or the complement thereof, and wherein the nucleic acid is capable of modulating transcription of a gene operably linked to the nucleic acid that encodes a CD36L1 receptor. The nucleic acid is disclosed to be capable of activating or enhancing transcription of this gene. Antisense compounds are only generally disclosed. Nowhere does this patent teach or suggest antisense compounds from 15 to 50 nucleobases in length that target specific regions of the CD36L1 nucleic acid molecule of SEQ ID NO: 3 as

claimed. In order to anticipate a claim, the reference cited must teach each and every limitation of the claims (MPEP 2131). Accordingly, this patent fails to teach the limitations of the claims and cannot anticipate the instant invention. Withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 1-10 and 12-14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Acton et al. (US Patent No. 5,965,790), in view of Calvo et al. (1993) and Baracchini et al. (US Patent No. 5,801,154). The Examiner suggests that it would have been *prima facie* obvious to one of ordinary skill to make antisense to inhibit CD36L1 because antisense inhibition was taught by Acton et al., the sequence of the gene was provided by Calvo et al., and Baracchini teach the desirability of modifying antisense compounds. The Examiner suggests one of skill would have been motivated to create such compounds due to the teaching of Acton et al. regarding the significant of this gene in disease and that Baracchini teach the need for modified oligonucleotides. The Examiner suggests one of skill would have had an expectation of success based on the teachings of Acton et al. and Baracchini et al. Applicants respectfully traverse this rejection.

At the outset, claim 1 and its dependent claims have been amended as discussed *supra* to recite antisense compounds targeted to specific regions of a nucleic acid molecules encoding CD36L1 of SEQ ID NO: 3.

As discussed *supra*, Acton et al. teach only the general idea of using antisense compounds to inhibit expression of CD36L1. No actual inhibition expression using antisense is disclosed or shown. Further, nowhere does this reference teach or suggest antisense compounds targeted to CD36L1 nucleic acid molecules as claimed, including specific regions of CD36L1 of SEQ ID NO: 3. Therefore, this primary reference fails to teach the limitations of the claims.

The secondary references cited fail to overcome the deficiencies in teaching of the primary references.

Calvo et al. (1993) discloses the sequence of CD36L1. Nowhere does this reference teach or suggest antisense compounds of any type targeted to CD36L1 nucleic acid molecules as claimed, including specific regions of CD36L1. Therefore, this reference also fails to teach the limitations of the claims as amended.

Baracchini et al. (US Patent 5,801,154) teaches methods of modifying antisense oligonucleotides to enhance activity. However, nowhere does this patent teach or suggest antisense oligonucleotides

8 to 50 nucleobases in length targeted to CD36L1 nucleic acid molecules, or any region of a CD36L1 nucleic acid molecule.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as amended, which claim antisense compounds targeted to specific regions of a nucleic acid molecule encoding CD36L1, and thus cannot render the instant claimed invention obvious. Moreover, a mere teaching of the concept of antisense for a gene does not give one the expectation of success for using antisense as disclosed in the instant invention. Withdrawal of this rejection is therefore respectfully requested.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 11 and 16-20 have been canceled without prejudice.

The claims have been amended as follows:

1. (amended) A compound 8 to 50 nucleobases in length targeted to a 5'-untranslated region, a start codon region, a coding region, a stop codon region, or a 3'-untranslated region of a nucleic acid molecule encoding CD36L1 of ~~(~~SEQ ID NO: 3~~)~~, an exon:exon junction region of a nucleic acid molecule encoding CD36L1 of SEQ ID NO: 12, a 3'-untranslated region of a nucleic acid molecule encoding CD36L1 of SEQ ID NO: 10, an exon:intron junction region, an intron 9 region, an intron 10 region, an intron:exon junction region, an intron 12 region, or an intron 13 region of a nucleic acid molecule encoding CD36L1 of SEQ ID NO: 13, wherein said compound specifically hybridizes with ~~said nucleic acid molecule encoding CD36L1~~ one of said regions and inhibits the expression of CD36L1.

15. (amended) A method of inhibiting the expression of CD36L1 in cells or tissues comprising contacting said cells or tissues *in*

vitro with the compound of claim 1 so that expression of CD36L1 is inhibited.